Amendments to the Specification

Please delete the original sequence listing from the specification and replace it with the substitute sequence listing filed with this submission.

Please replace Figures 1C and 1D with the Replacement Drawing Sheets accompanying this submission.

In addition, please amend the specification as shown:

Please delete the paragraph on page 6, lines 11-28 and replace it with the following paragraph:

In a preferred embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of $X_1X_2X_3X_4TQX_5PSX_6X_7SX_8X_9X_{10}GX_{11}X_{12}X_{13}X_{14}IX_{15}CX_{16}X_{17}SX_{18}X_{19}IX_{20}X_{21}X_{22}X_{23}X_{24}WYQQX_{25}PG$ $X_{26}APX_{27}X_{28}LX_{29}YX_{30}X_{31}X_{32}X_{33}LX_{34}X_{35}GVX_{36}X_{37}RFSGX_{38}X_{39}SGTDFX_{40}LTIX_{41}X_{42}LQX_{43}X_{44}DX_{45}A$ $X_{46}YYCQQX_{47}X_{48}X_{49}X_{50}PX_{51}TFGX_{52}GTKX_{53}X_{54}IK$ **(SEQ ID NO: 338)**, wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein X_1 is D, E or A; X_2 is I, or T; X_3 is V, E, K, R, Q, or T; X_4 is M, or L; X_5 is S, or T, X_6 is S, or T; X_7 is L, or V; X_8 is A, or V; X_9 is S, or T; X_{10} is P, V, L, A, or I; X_{11} is E, or D; X_{12} is R, or T; X_{13} is A, or V I; X_{14} is T, or A; X_{15} is T, S, or A; X_{16} is S, R, N, K, H, or Q; X_{17} is A, or S; X_{18} is Q, or R; X_{19} is S, D, A, or P; X_{20} is S, G, R, T, or Y; X_{21} is T, N, S, D, or K; X_{22} is Y, or D; X_{23} is L, or I; X_{24} is A, N, or T; X_{25} is K, or I; X_{26} is Q, K, T, or I; X_{27} is R, K, Q, N, H, S, or E; X_{28} is V, or L; X_{29} is I, or V; X_{30} is F, A, G , D, or S; X_{31} is A , or T; X_{32} is S, or T; X_{33} is N, S, R, or T; X_{34} is A, H, or Q; X_{35} is S , or G; X_{36} is P, T; X_{37} is S, N, D, G, or Y; X_{38} is S, or T; X_{39} is G, or R; X_{40} is T, or A; X_{41} is S, or R; X_{42} is S, or R; X_{43} is P, or A; X_{44} is E , or D; X_{45} is F, V, or S; X_{46} is V, T, I , A , or S; X_{47} is Y, or S; X_{48} is S, Y, or N; X_{49} is S , or T; X_{50} is T, V, A, P, K, G, S, or I; X_{51} is W , or Y; X_{52} is Q , or G; X_{53} is V, or L; and X_{54} is E, D , or A.

Please delete the paragraph on page 7, lines 1-12 and replace it with the following paragraph:

In another preferred embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of $X_1X_2X_3LTQPPSX_4SX_5TPGQX_6VTISCSGX_7X_8SNX_9GX_{10}NX_{11}VX_{12}WYQQX_{13}PGX_{14}APKX_{15}LX_{16}Y$ $X_{17}NX_{18}X_{19}RPSGVPX_{20}RX_{21}SGSX_{22}SX_{23}TSASLAISGLX_{24}SEDEADYYCX_{25}X_{26}WDDSLX_{27}GYVF$

$GX_{28}GTX_{29}LTVL$ **(SEQ ID NO: 339)**, wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein X_1 is Q L, or N; X_2 is P A F, or S; X_3 is V, or M; X_4 is A, or T; X_5 is G, or A; X_6 is R, or S; X_7 is S, or T; X_8 is S, T Y, or N; X_9 is I , or V; X_{10} is S, or R; X_{11} is S, P, N, A, or T; X_{12} is N, T , or Y; X_{13} is L, or F; X_{14} is T, or A; X_{15} is V, L, or F; X_{16} is M, or I; X_{17} is G, T, or S; X_{18} is N, or D; X_{19} is Q, or E; X_{20} is D, or E; X_{21} is F, or L; X_{22} is K, or R; X_{23} is G, or A; X_{24} is Q, L, or R; X_{25} is A, or G; X_{26} is A, S, or T; X_{27} is N, S, or T; X_{28} is T, or A; and X_{29} is K, or Q.

Please delete the paragraph on page 7, line 23 to page 8, line 6 and replace it with the following paragraph:

In yet another preferred embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has V_H comprising the amino acid sequence of $X_1X_2QLVX_3SGGGX_4VQPGGX_5LRLX_6CAX_7SGX_8X_9X_{10}X_{11}X_{12}X_{13}GX_{14}NWX_{15}RQAPGKGX_{16}EWV$ $GWX_{17}NTX_{18}X_{19}GX_{20}X_{21}TYX_{22}X_{23}X_{24}FX_{25}RRX_{26}TX_{27}SX_{28}X_{29}X_{30}SKX_{31}X_{32}X_{33}YLQX_{34}NSLRAEDTA$ $VYYCAX_{35}YPX_{36}YYGX_{37}SHWYFDVWX_{38}QGTLVTVSS$ **(SEQ ID NO: 340)**, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively, whereas the rest of the region is designated as framework according to Kabat nomenclature, and wherein X_1 is E, or Q; X_2 is V, or G; X_3 is Q, or E; X_4 is V, or L; X_5 is S, or T; X_6 is S T, or R; X_7 is A, or V; X_8 is Y, or F; X_9 is T, D, N, S, or A; X_{10} is F, or L; X_{11} is T, D, Y, A, S, or N; X_{12} is N, H, or S; X_{13} is Y, or F; X_{14} is M, L, I, or V; X_{15} is I, V, or L; X_{16} is L, or P; X_{17} is I, or V; X_{18} is Y, or N; X_{19} is T, or N; X_{20} is E, or A; X_{21} is P, T, or S; X_{22} is A, or V; X_{23} is A, H, Q, P, D, or E; X_{24} is D, or E; X_{25} is K, or T; X_{26} is V, F, or L; X_{27} is F, or I; X_{28} is L, or R; X_{29} is D, or N; X_{30} is T, or N; X_{31} is S, or N; X_{32} is T, Q, P, or K; X_{33} is A, V, or P; X_{34} is L, or M; X_{35} is K, or R; X_{36} is H, or Y; X_{37} is S, R, or T; and X_{38} is G, or A.

Please delete the paragraph on page 9, lines 17-21 and replace it with the following paragraph:

In yet another embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has a framework region (FR) CDR3 in the V_L region (V_L/FR) comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:229-269 **and 351-401**, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:232**, 351, 355 and 353;**[[,]] 235**, 354, 360 and 353;**[[,]] 237**, 361, 359 and 362;**[[,]] 251 **and 374-376;**[[,]] 255**, 371, 381 and 380;**[[,]] 263**, 389 and 391-392;**[[,]] and 265**, 395-396 and 394**.

Please delete the paragraph on page 10, lines 5-9 and replace it with the following paragraph:

In one embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H/CDR2) comprising the amino acid sequence of $WX_1NTX_2X_3GEX_4TYX_5X_6X_7FX_8R$ **(SEQ ID NO: 341)**, wherein X_1 is I, or V; X_2 is Y, or N; X_3 is T, or N; X_4 is P, T, or S; X_5 is A, or V; X_6 is A, Q, P, H, D, or E; X_7 is D, or E; and X_8 is K, or T

Please delete the paragraph on page 10, lines 16-18 and replace it with the following paragraph:

In one embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H/CDR3) comprising the amino acid sequence of $KYPX_1YYGX_2SHWYFDV$ **(SEQ ID NO: 342)**, wherein X_1 is Y, or H, and X_2 is R.

Please delete the paragraph on page 10, line 25 to page 11, line 2 and replace it with the following paragraph:

In one embodiment, a monoclonal antibody is provided that specifically binds to a human VEGF and has FR in the V_H region (V_H/FR) comprising the amino acid sequence of $X_1VQLVX_2SGGGX_3VQPGGX_4LRLX_5CAX_6S$ **(SEQ ID NO: 343)**/CDR1/$WX_7RQAPGKGLEWVG$ **(SEQ ID NO: 344)**/CDR2/$RX_8TX_9SX_{10}DX_{11}SKX_{12}X_{13}X_{14}YLQX_{15}NSLRAEDTAVYYCA$ **(SEQ ID NO: 345)**/CDR3/$WX_{16}QGTLVTVSS$ **(SEQ ID NO: 346)**, wherein X_1 is E, or Q; X_2 is Q, or E; X_3 is V, or L; X_4 is S, or T; X_5 is S, T, or R; X_6 is A, or V; X_7 is I, or V; X_8 is F, or V; X_9 is F, or I; X_{10} is L, or R is X_{11} is T, or N; X_{12} is S, or N; X_{13} is T, Q, or K; X_{14} is A, or V; X_{15} is M, or L; and X_{16} is G, or A.

Please delete the paragraphs on page 12, lines 4 -14 and replace them with the following paragraphs:

Figure 1A shows an AA-PVP profile of V_L hit variants designed by using the inventive methodology *in silico.* **The AA-PVP of the VL chain uses the humanized VL (SEQ ID NO:1) by Baca et al. (1997) J Biol Chem 272: 10678-10684 as a reference sequence. The dot indicates the same amino acid as reference. CDRs are indicated in bold letters underlined. Figure 1A discloses residues 1-97 of SEQ ID NO: 1 and SEQ ID NO: 349.**

Figure 1B shows an AA-PVP profile of V_H hit variants designed by using the inventive methodology *in silico.* **The AA-PVP of the VH chain uses the humanized VH (SEQ ID NO:55)**

by Baca et al. (1997), supra as a reference sequence. The dot indicates the same amino acid as reference. CDRs are indicated in bold letters underlined. Figure 1 B discloses residues 1-114 of SEQ ID NO: 55 and SEQ ID NO: 350.

Figure 1C shows amino acid sequences of full-length VL **(SEQ ID NOS:1- 54 and SEQ ID NO: 284), VL/CDRs (CDR1 SEQ ID NOS: 164 - 194; CDR2 SEQ ID NOS: 195 - 209; CDR3 SEQ ID NOS: 210 - 228),** and VL/FR **sequences** of certain embodiments of the antibodies according to the present invention. **The VL/FR sequences are set forth as consecutive framework segments (i.e., FR1, FR2, FR3 and FR4) and CDR (ie., CDR1, CDR2 and CDR3) region placeholders. For example, the first VL/FR sequence set forth in Figure 1 C comprises a FR1 sequence (SEQ ID NO: 229) a placeholder for a CDR1 sequence, a FR2 sequence (SEQ ID NO: 351), a placeholder for CDR2, a FR3 sequence (SEQ ID NO: 352), a placeholder for CDR3, and a FR4 sequence (SEQ ID NO: 353).**

Figure 1D shows amino acid sequences of full-length VH **(SEQ ID NOS: 55 – 110, SEQ ID NO: 283 and SEQ ID NOS: 285 – 310), VH/CDRs (CDR1 SEQ ID NOS: 111 – 135; CDR2 SEQ ID NOS: 136-156; CDR3 SEQ ID NOS: 311-337),** and VH/FR **sequences** of certain embodiments of the antibodies according to the present invention. **The VH/FR sequences are set forth as consecutive framework segments (ie., FR1, FR2, FR3 and FR4) and CDR (i.e., CDR1, CDR2 and CDR3) placeholders, according to the same format described above for the VL/FR sequences set forth in Figure 1C.**

Please delete the paragraph on page 16, line 29 to page 18, line 17 and replace it with the following paragraph:

In a preferred embodiment, an anti-VEGF antibody is provided that has a light chain variable region comprising the amino acid sequence of:
$X_1X_2X_3X_4TQX_5PSX_6X_7SX_8X_9X_{10}GX_{11}X_{12}X_{13}X_{14}IX_{15}CX_{16}X_{17}SX_{18}X_{19}IX_{20}X_{21}X_{22}X_{23}X_{24}WYQQX_{25}PG$
$X_{26}APX_{27}X_{28}LX_{29}YX_{30}X_{31}X_{32}X_{33}LX_{34}X_{35}GVX_{36}X_{37}RFSGX_{38}X_{39}SGTDFX_{40}LTIX_{41}X_{42}LQX_{43}X_{44}DX_{45}A$
$X_{46}YYCQQX_{47}X_{48}X_{49}X_{50}PX_{51}TFGX_{52}GTKX_{53}X_{54}IK$ **(SEQ ID NO: 338)**, wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein the position designated as "X" could be amino acids listed below:
X_1 : D, E or A
X_2 : I, or T

X_3 : V, E, K, R, Q, or T

X_4 : M, or L

X_5 : S, or T

X_6 : S, or T

X_7 : L, or V

X_8 : A, or V

X_9 : S, or T

X_{10} : P, V, L, A, or I

X_{11} : E, or D

X_{12} : R, or T

X_{13} : A, or V I

X_{14} : T, or A

X_{15} : T, S, or A

X_{16} : S, R, N, K, H, or Q

X_{17} : A, or S

X_{18} : Q, or R

X_{19} : S, D, A, or P

X_{20} : S, G, R, T, or Y

X_{21} : T, N, S, D, or K

X_{22} : Y, or D

X_{23} : L, or I

X_{24} : A, N, or T

X_{25} : K, or I

X_{26} : Q, K, T, or I

X_{27} : R, K, Q, N, H, S, or E

X_{28} : V, or L

X_{29} : I, or V

X_{30} : F, A, G , D, or S

X_{31} : A , or T

X_{32} : S, or T

X_{33} : N, S, R, or T

X_{34} : A, H, or Q

X_{35} : S , or G

X_{36} : P, T

X_{37} : S, N, D, G, or Y

X_{38} : S, or T

X_{39} : G, or R

X_{40} : T, or A

X_{41} : S, or R

X_{42} : S, or R

X_{43} : P, or A

X_{44} : E , or D

X_{45} : F, V, or S

X_{46} : V, T, I , A , or S

X_{47} : Y, or S

X_{48} : S, Y, or N

X_{49} : S , or T

X_{50} : T, V, A, P, K, G, S, or I

X_{51} : W , or Y

X_{52} : Q , or G

X_{53} : V, or L

X_{54}: E, D , or A.

Please delete the paragraph on page 18, line 22 to page 19, line 18 and replace it with the following paragraph:

In another preferred embodiment, an anti-VEGF antibody is provided that has a light chain variable region comprising the amino acid sequence of:
$X_1X_2X_3$LTQPPSX_4SX_5TPGQX_6VTISCS$\underline{GX_7X_8SNX_9GX_{10}NX_{11}VX_{12}}$WYQQ$X_{13}PGX_{14}APKX_{15}LX_{16}$Y
$\underline{X_{17}NX_{18}X_{19}RPS}GVPX_{20}RX_{21}SGSX_{22}SX_{23}$TSASLAISGL$X_{24}$SEDEADYYC$\underline{X_{25}X_{26}WDDSLX_{27}GYVF}$
GX_{28}GTX_{29}LTVL **(SEQ ID NO: 339)**, wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein the position designated as "X" could be amino acids listed below:

X_1 : Q L, or N

X_2 : P A F, or S

X_3 : V, or M

X_4 : A, or T

X_5 : G, or A

X_6 : R, or S

X_7 : S, or T

X_8 : S, T Y, or N

X_9 : I , or V

X_{10} : S, or R

X_{11} : S, P, N, A, or T

X_{12} : N, T , or Y

X_{13} : L, or F

X_{14} : T, or A

X_{15} : V, L, or F

X_{16} : M, or I

X_{17} : G, T, or S

X_{18} : N, or D

X_{19} : Q, or E

X_{20} : D, or E

X_{21} : F, or L

X_{22} : K, or R

X_{23} : G, or A

X_{24} : Q, L, or R

X_{25} : A, or G

X_{26} : A, S, or T

X_{27} : N, S, or T

X_{28} : T, or A

X_{29} : K, or Q.

Please delete the paragraphs on page 19, line 32 to page 22, line 16 and replace them with the following paragraphs:

In yet another preferred embodiment, an anti-VEGF antibody is provided that has a heavy chain variable region comprising the amino acid sequence of:
X_1X_2QLVX_3SGGGX_4VQPGGX_5LRLX_6CAX_7S$\underline{GX_8X_9X_{10}X_{11}X_{12}X_{13}GX_{14}N}WX_{15}$RQAPGKG$X_{16}$EWV
G$\underline{WX_{17}NTX_{18}X_{19}GX_{20}X_{21}TYX_{22}X_{23}X_{24}FX_{25}R}RX_{26}TX_{27}SX_{28}X_{29}X_{30}SKX_{31}X_{32}X_{33}YLQX_{34}$NSLRAEDTA
VYYCA$\underline{X_{35}YPX_{36}YYGX_{37}SHWYFDV}WX_{38}$QGTLVTVSS **(SEQ ID NO: 340)**, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively, whereas the rest of the region is designated as framework according to Kabat nomenclature, and wherein the position designated as "X" could be amino acids listed below:

X_1 : E, or Q

X_2 : V, or G

X_3 : Q, or E

X_4 : V, or L

X_5 : S, or T

X_6 : S T, or R

X_7 : A, or V

X_8 : Y, or F

X_9 : T, D, N, S, or A

X_{10} : F, or L

X_{11} : T, D, Y, A, S, or N

X_{12} : N, H, or S

X_{13} : Y, or F

X_{14} : M, L, I, or V

X_{15} : I, V, or L

X_{16} : L, or P

X_{17} : I, or V

X_{18} : Y, or N

X_{19} : T, or N

X_{20} : E, or A

X_{21} : P, T, or S

X_{22} : A, or V

X_{23} : A, H, Q, P, D, or E

X_{24} : D, or E

X_{25} : K, or T

X_{26} : V, F, or L

X_{27} : F, or I

X_{28} : L, or R

X_{29} : D, or N

X_{30} : T, or N

X_{31} : S, or N

X_{32} : T, Q, P, or K

X_{33} : A, V, or P

X_{34} : L, or M

X_{35} : K, or R

X_{36} : H, or Y

X_{37} : S, R, or T

X_{38} : G, or A.

In yet another preferred embodiment, an anti-VEGF antibody is provided that has a heavy chain variable region comprising the amino acid sequence of:

X_1X_2QLVX_3SGGGX_4VQPGGX_5LRLX_6CAX_7S$\underline{GX_8X_9X_{10}X_{11}X_{12}X_{13}GX_{14}}NWX_{15}$RQAPGKG$X_{16}$EWV G$\underline{WX_{17}NTX_{18}X_{19}GX_{20}X_{21}TYX_{22}X_{23}X_{24}FX_{25}}RRX_{26}TX_{27}SX_{28}X_{29}X_{30}SKX_{31}X_{32}X_{33}YLQX_{34}$NSLRAEDTA VYYCA$\underline{X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}X_{42}X_{43}X_{44}X_{45}YX_{46}DX_{47}}WX_{48}$QGTLVTV **(SEQ ID NO: 347)**, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively, whereas the rest of the region is designated as framework according to Kabat nomenclature, and wherein the position designated as "X" could be amino acids listed below:

X_1 : E, or Q

X_2 : V, or G

X_3 : Q, or E

X_4 : V, or L

X_5 : S, or T

X_6 : S T, or R

X_7 : A, or V

X_8 : Y, or F

X_9 : T, D, N, S, or A

X_{10} : F, or L

X_{11} : T, D, Y, A, S, or N

X_{12} : N, H, or S

X_{13} : Y, or F

X_{14} : M, L, I, or V

X_{15} : I, V, or L

X_{16} : L, or P

X_{17} : I, or V

X_{18} : Y, or N

X_{19} : T, or N

X_{20} : E, or A

X_{21} : P, T, or S

X_{22} : A, or V

X_{23} : A, H, Q, P, D, or E

X_{24} : D, or E

X_{25} : K, or T

X_{26} : V, F, or L

X_{27} : F, or I

X_{28} : L, or R

X_{29} : D, or N

X_{30} : T, or N

X_{31} : S, or N

X_{32} : T, Q, P, or K

X_{33} : A, V, or P

X_{34} : L, or M

X_{35} : K R, or H

X_{36} : Y A D, or S

X_{37}: P R S, or G

X_{38} : Y H, or D

X_{39} : Y, or F

X_{40} : Y N S, or H

X_{41} : G , or S

X_{42} : S, T, R, G, or A

X_{43} : S, Y, C, or T

X_{44} : H, P, C, N, Q, or S

X_{45} : W, Q, or C

X_{46} : F , or L

X_{47} : V, L, or Y

X_{48} : G, or A.

Please delete the paragraph on page 24, line 25 to page 35, line 10 and replace it with the following paragraph:

In yet another embodiment, the invention provides an anti-VEGF antibody that preferably contains the framework regions of the light chain variable domain comprising the amino acid sequence of one of the following: SEQ ID NO:229 **and 351-353**, SEQ ID NO:230, **354-355 and 353**, SEQ ID NO:231, **356-357 and 353,** SEQ ID NO:233, **358, 355 and 353**, SEQ ID NO:234, **354, 359 and 353**, SEQ ID NO:236, **351, 360 and 353**, SEQ ID NO:238, **363, 355 and 353**, SEQ ID NO:239, **363-364 and 353**, SEQ ID NO:240 **and 351-353**, SEQ ID NO:241, **351, 360 and 353**, SEQ ID NO:242, **354, 360 and 353**, SEQ ID NO:243, **354, 365 and 353**, SEQ ID NO:244,

366-367 and 353, SEQ ID NO:245**, 368-369 and 353**, SEQ ID NO:246**, 354-355 and 370**, SEQ ID NO:247**, 361 and 352-353**, SEQ ID NO:248**, 356, 359 and 353**, SEQ ID NO:249**, 361, 360 and 353**, SEQ ID NO:250 **and 371-373**, SEQ ID NO:252**, 377-378 and 376**, SEQ ID NO:253 **and 371-373**, SEQ ID NO:254**, 379, 375 and 380**, SEQ ID NO:256**, 382 and 375-376**, SEQ ID NO:257**, 383 and 375-376**, SEQ ID NO:258**, 383, 375 and 373**, SEQ ID NO:259**, 384, 375 and 380**, SEQ ID NO:260**, 385, 375 and 373**, SEQ ID NO:261 **and 386-388**, SEQ ID NO:262**, 389-390 and 388**, SEQ ID NO:264**, 393, 387 and 394**, SEQ ID NO:266 **and 397-399**, SEQ ID NO:267**, 400-401 and 394**, SEQ ID NO:268**, 400-401 and 394**, and SEQ ID NO:269**, 397, 387 and 394**; further preferably contains the framework regions of the light chain variable domain comprising the amino acid sequence of one of the following: SEQ ID NO:232**, 356-357 and 353**, SEQ ID NO:235**, 354, 360 and 353**, SEQ ID NO:237**, 361, 359 and 362**, SEQ ID NO:251 **and 374-376**, SEQ ID NO:255**, 371, 381 and 380**, SEQ ID NO:263**, 389 and 391-392**, and SEQ ID NO:265**, 395-396 and 394**. Such preferred framework region sequence of light chain variable region may be combined with CDR regions of preferred light chain, or of other light chain, and the preferred heavy chain variable region sequence or with other heavy chain variable region sequence, provided that the antibody so produced binds to human VEGF with desired affinity.

Please delete the paragraph on page 26, lines 1-12 and replace it with the following paragraph:

In one embodiment, the invention provides an anti-VEGF antibody that preferably contains CDR2 of the heavy chain variable domain comprising the amino acid sequence of one of the following: $WX_1NTX_2X_3GEX_4TYX_5X_6X_7FX_8R$ **(SEQ ID NO: 341)**, wherein the position designated as "X" could be amino acids listed below:

X_1: I, or V

X_2: Y, or N

X_3: T, or N

X_4: P, T, or S

X_5: A, or V

X_6: A, Q, P, H, D, or E

X_7: D, or E

X_8: K, or T

Please delete the paragraphs on page 26, line 24 to page 27, line 21 and replace them with the following paragraphs:

In one embodiment, the invention provides an anti-VEGF antibody that contains CDR3 of the heavy chain variable domain comprising the amino acid sequence: $KYPX_1YYGX_2SHWYFDV$ **(SEQ ID NO: 342)**, wherein the position designated as "X" could be amino acids listed below: X_1: Y, or H, and X_2: R.

Preferably, the anti-VEGF antibody has CDR3 of the heavy chain variable domain comprising the amino acid sequence of one of SEQ ID NOs:311-337, and the following sequences:

CAHSRHYYGSSPQYFDV
CAKYGYYYGSSHWYFDV
CAKYPHYYGASHWYFDV
CAKYPHYYGGCHWYFDV
CAKYPHYYGGSHWYFDV
CAKYPHYYGGYNQYFDV
CAKYPHYYGRSHWYFDV
CAKYPHYYGRSQWYLDV
CAKYPHYYSRTCQYFDV
CAKYPHYYSSSHWYFDV
CAKYPYFYGSSHWYFDV
CAKYPYYHGSSHWYFDV
CAKYPYYNGSSHWYFDV
CAKYPYYNSTSHWYFDV
CAKYPYYSGTSHWYFDV
CAKYPYYSGTSHWYFDY
CAKYPYYYGRSHWYFDV
CAKYPYYYGSSHWYFDV
CAKYPYYYGSSSWYFDV
CAKYPYYYSTSHWYFDV
CAKYRDFNGSSHWYFDV
CAKYSYYYGSSHWYFDV
CARARHYYGSSHCYFDL
CARDSHYYGSSHQYFDL
CAKYPHYYGTSHWYFDV
CAKYPHYYGSSHWYFDV
CAKYPYYYGTSHWYFDV.

Please delete the paragraph on page 27, line 28 to page 28, line 8 and replace it with the following paragraph:

In one embodiment, the invention provides an anti-VEGF antibody that preferably contains the framework region of the heavy chain variable domain comprising the amino acid sequences of one of the following: X_1VQLVX_2SGGGX_3VQPGGX_4LRLX_5CAX_6S **(SEQ ID NO: 343)**/CDR1/WX_7RQAPGKGLEWVG **(SEQ ID NO: 344)**/CDR2/RX_8TX_9SX_{10}DX_{11}SK$X_{12}X_{13}X_{14}$YLQX_{15}NSLRAEDTAVYYCA **(SEQ ID NO: 345)**/CDR3/WX_{16}QGTLVTVSS **(SEQ ID NO: 346)**, wherein the position designated as "X" could be amino acids listed below:

X_1 : E, or Q

X_2 : Q, or E

X_3 : V, or L

X_4 : S, or T

X_5 : S, T, or R

X_6 : A, or V

X_7 : I, or V

X_8 : F, or V

X_9 : F, or I

X_{10} : L, or R

X_{11} : T, or N

X_{12} : S, or N

X_{13} : T, Q, or K

X_{14} : A, or V

X_{15} : M, or L

X_{16} : G, or A.

Please delete the paragraph on page 58, lines 17-28 and replace it with the following paragraph:

The lead sequence includes V_H CDR3 of the parental anti-VEGF antibody and a few amino acid residues from the adjacent framework regions CAKYPHYYGSSHWYFDVWG **(SEQ ID NO: 348)**. A hit library was constructed by searching and selecting hit amino acid sequences to V_H CDR3 from a sequence database. Variant profile was built to list all variants at each position based on the hit library and filtered with certain cutoff value to reduce of the size of the resulting hit variant library within computational or experimental limit. Variant profiles were also built in order

to facilitate i) the sampling of the sequence space that covers the preferred region in the fitness landscape; ii) the partitioning and synthesis of degenerate nucleic acid libraries that target the preferred peptide ensemble sequences; iii) the experimental screening of the antibody libraries for the desired function; and iv) the analysis of experimental results with feedback for further design and optimization.

Please delete the paragraph on page 64, lines 4-7 and replace it with the following paragraph:

The amino acid sequence of the framework fr123 region of the murine anti-VEGF antibody is:

EIQLVQSGPELKQPGETVRISCKASWVKQAPGKGLKWMGRFTFSLETSASTAYLQISNLKNDD TATYFCA **(SEQ ID NO: 292)**.

Please delete Table 1 and the following paragraph on page 74, line 1 to page 75, line 8 and replace them with the following table and paragraph:

Table 1: Primers for Vk and Vl amplification

		SEQ ID NO:
Vk	ATTAATGGATCCGMCATCCRGWTGACCCAGTCTCC	421
	ATTAATGGATCCGATRTTGTGATGACYCAGWCTCC	422
	ATTAATGGATCCGAAATWGTGWTGACRCAGTCTCC	423
	ATTAATGGATCCGACATCGTGATGACCCAGTCTCC	424
	ATTAATGGATCCGAAACGACACTCACGCAGTCTCC	425
	ATTAATGGATCCGAAATTGTGCTGACTCAGTCTCC	426
Vl	ATTAATGGATCCCAGTCTGTGYTGACKCAGCC	427
	ATTAATGGATCCCAGTCTGCCCTGACTCAGCC	428
	ATTAATGGATCCTCCTATGAGCTGACWCAGCyAC	429
	ATTAATGGATCCTCTTCTGAGCTGACTCAGGAC	430
	ATTAATGGATCCCTGCCTGTGCTGACTCAGCC	431
	ATTAATGGATCCCAGCYTGTGCTGACTCAATC	432
	ATTAATGGATCCCAGSCTGTGCTGACTCAGCC	433
	ATTAATGGATCCAATTTTATGCTGACTCAGCCC	434
	ATTAATGGATCCCAGRCTGTGGTGACYCAGGAG	435
	ATTAATGGATCCCAGGCAGGGCTGACTCAGCC	436
Jk	TTAATTGCGGCCGCTTTGATYTCCASCTTGGTCCC	437
	TTAATTGCGGCCGCTTTGATATCCACTTTGGTCCC	438
	TTAATTGCGGCCGCTTTAATCTCCAGTCGTGTCCC	439
Jl	TTAATTGCGGCCGCTAGGACGGTSASCTTGG	440
	TTAATTGCGGCCGCGAGGACGGTCAGCTGGG	441

4. Expression of Soluble Antibody Fragments

Soluble antibody fragments in the format of single chain variable fragment (scFv) can be generated in prokaryotic (E. coli) and eukaryotic (yeast) expression systems for the purpose of biophysical analysis. Construction of scFv includes a VH fragment and a VL fragment connected by a linker of $(G_4S)_3$ **(SEQ ID NO: 442)** as described in previous studies (Barbas et al., Phage display: a laboratory manual, Cold Spring Harbor Laboratory Press, 2001). Expression vector used for prokaryotic expression is illustrated in Figure 7. Competent bacterial cells, e.g., BL21, were prepared and transformed with a vector that carries the antibody fragment according to methods known in the art (Sambrook, Fritsch and Maniatis, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Press, Cold Spring Harbor, N.Y., (1989); Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988). The transformed cells are cultured under conditions suitable for protein expression. Such conditions are well known to artisans in the field and hence are not detailed herein. The expressed antibodies are harvested using conventional methods known in the art and used for further analysis. Expression in yeast was performed using Pichia expression kit purchased from Invitrogen and according to manufacturer's instruction. All antibodies were tagged with a HA-His6 tag **(SEQ ID NO: 443)** at C-terminus, and purified by NTA and Superdex 75 columns. In order to determine the purity and expression yield of antibody fragments, 20 ul of purified proteins are analyzed by SDS-PAGE gel, and visualized by staining with Coomassie Brilliant Blue R-250.

Please delete the original sequence listing from the specification and replace it with the substitute sequence listing filed with this submission, at the end of the Detailed Description before the claims.